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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,317	07/13/2006	Frank Leenders	14836-53313	4625

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EXAMINER	
UNDERDAHL, THANE E	
ART UNIT	**PAPER NUMBER**
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,317	LEENDERS ET AL.	
	Examiner	Art Unit	
	Thane Underdahl	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Restriction/Election

Applicant's response, with traverse, to the Restriction/Election requirement filed on 2/26/07 is acknowledged. The applicant elected Group I which includes claims 1-7.

The applicant argues that group I and group II are not distinct inventions. That group I is drawn to a pharmaceutical preparation and group II is to a method of use of this pharmaceutical preparation. However the reference cited in restriction requirement by Anderson et al. (CANCER, Vol 83(7) October 1, 1998,) shows that, since the claims are written with such broad terms as "a compound having glutaminase activity" and "antineoplastic agent", the pharmaceutical preparation and the method of use are known in the art. As such they lack a special technical feature to join them and are then considered distinct as written.

Applicant further alleges that there would be no burden on the examiner in examining all of the claims at once, relying on M.P.E.P. §802.02. Chapter 800, however, is limited to a discussion of the subject of restriction and double patenting under Title 35 of the United States Code and Title 37 of the Code of Federal Regulations as it relates to national applications filed under 35 U.S.C. 111(a). The discussion of unity of invention under the Patent Cooperation Treaty Articles and Rules as it is applied as an International Searching Authority, International Preliminary Examining Authority, and in applications entering the National Stage under 35 U.S.C. 371 as a Designated or Elected Office in the U.S. Patent and Trademark Office is covered in M.P.E.P. §1850 and is dictated by PCT Rules 13.1 and 13.2. See M.P.E.P. §801. Burden is not a consideration in a finding of lack of inventive unity; rather, according to M.P.E.P. §1850, the only consideration is whether the inventions share a special technical feature.

Nevertheless, the applicant traverses the restriction requirement on the grounds that no burden exists in examiner the application. However the examiner is burdened to search both relevant patent and patent applications as well as non-patent literature in the examination of the claims.

Therefore, the Restriction/Election requirement is therefore made FINAL and the claims 1-7 will now be examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims are drawn to a "pharmaceutical preparation". This term is in definite because the word "preparation" can be a verb on noun depending on the context. It is not clear if the claims are drawn to a composition or method of making. Clarification is required. In the interest of compact prosecution, the claims will be examined as compositions.

Claims 3 and 4 contain the word "preferably" which make it unclear if the following limitations are necessary or optional. Clarification is required.

Similarly claim 7 recites the word "optionally" which is indefinite since it does not provide a specific limitation to the claim (M.P.E.P. § 2111.04). In the interest of compact prosecution, the claim will read "A pharmaceutical preparation from claim 1 comprised in a pharmaceutically acceptable carried for oral and parenteral administration"

Claims 5 and 6 are also indefinite since it is unclear if the lists of doxorubicin, daunomycin, actinomycin D or/and mitoxantrone as well as the list of cis-platinum, oxaliplatinum or/and carboplatinum are the species of anthracyclines and platinum complexes mention in claim 1 or are compounds further comprised in claim 1. Clarification is required. In the interest of compact prosecution, these lists will be read as Markush groups in which the species of anthracyclines or platinum complexes are selected.

Claim 1 is in improper Markush form. This claim has the Markush form of "at least one antineoplastic agent selected from A and B". A Markush group should be in the form "an agent selected from the group consisting of A, B, **and** C". Currently, it is not clear which species are included in the Markush group and which are not.

Claims 5 and 6 are also in improper Markush form. These claims have the Markush form of "Preparation...characterized in that in comprises A, B or/and C". A Markush group should be in the form "an agent selected from the group consisting of A, B, **and** C". Currently, it is not clear which species are included in the Markush group and which are not.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leskovar et al. (WO 89/09620 of PCT/EP89/00403). This reference is written in German. However it has a U.S. Patent Publication (US 2002/0094542) which is a 371 and as such is an English language equivalent document (see M.P.E.P., Appendix L, 35 U.S.C. 371 National stage: Commencement.) The Examiner will cite the U.S. Patent Publication for convenience, but the rejection remains over WO 89/09620.

These claims are to a combined pharmaceutical preparation comprising as active substances: (a) at least one compound having glutaminase activity (**GA**) and (b) at least one antineoplastic agent selected from platinum complexes and anthracyclines. Claim 2 limits claim 1 by teaching the compound having GA is glutaminase, glutaminase-asparaginase, glutaminase analog, derivative or modification of the same and is either of natural origin or is produced synthetically. Claim 3 limits that the compound with GA is from Pseudomonas. Claim 4 limit that the GA compound is modified. Claim 5 limits the type of anthracycline. Claim 7 teach the pharmaceutical preparation further comprises a pharmaceutically acceptable carrier for oral or parenteral administration.

Leskovar et al. teach a pharmaceutical preparation that comprises the Component A which includes anthracyclines such as doxorubicin and daunomycin that have been modified by conjugating them with antibodies (paragraphs 21-23). Leskovar et al. also teach that their pharmaceutical preparation can comprise antibody immunoconjugates of the enzymes asparaginase and glutaminase (paragraph 192). Leskovar et al. does not specifically teach the addition of both the anthracyclines and glutaminase enzymes in the same composition. However Leskovar et al. does teach that xenogeneic proteins can be admixed with Component A and either administered patenterally or orally (paragraph 25-26). One of ordinary skill in the art would recognize that that a composition of enzymes and anthracyclines would need to be mixed with a pharmaceutically acceptable carrier such as water to be administered patenterally or orally.

It would therefore have been obvious for the person of ordinary skill in the art to modify the invention of Leskovar et al. to combine an enzyme such as glutaminase with component A, which they teach as an anthracycline such as doxorubicin. Leskovar et al. provides express motivation and reasonable expectation of success by stating that "conjugates, composed of xenogeneous proteins...can be admixed to the component A" (paragraph 26).

Furthermore it would be obvious to combine the anthracycline and glutaminase since they are two components known for the same purpose (see M.P.E.P. § 2144.06). In this case the treatment of cancer (paragraph 140 and 192).

Leskovar et al. also does not teach that the compound having glutaminase activity is from *Pseudomonas*. This is a product by process claim since it defines the product as being made from a specific process or method.

However M.P.E.P. § 2113 states "product-by process claims" such as this "are not limited to the manipulations of the recited steps, only the structure implied by the steps" as cited below:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Therefore since Leskovar et al. teaches utilizing glutaminase, it would have been obvious at the time the invention was made to use any known glutaminase (regardless of the source) with a reasonable expectation of the same success found in using the glutaminase of Leskovar. Thus it would have been *prima facie* obvious to substitute any

glutaminase into the preparation of Leskovar absent any teaching of criticality for the specific enzyme claimed. Furthermore any glutaminase regardless of its source will perform the same chemical reaction and can therefore be used for the same purpose and it would be obvious for one of ordinary skill in the art to substitute one glutaminase for the other (M.P.E.P. § 2144.06).

Therefore, the invention as a whole would have been prima facie obvious at the time of filing in view of the reference listed above and as such claims 1-5 and 7 are not allowable.

Claim1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leskovar et al. (WO 89/09620 of PCT/EP89/00403) as applied to claim1-5 and 7 above, and further in view of Housman et al. (U.S. Patent # 6,200,754, 2001).

The details of clams 1-5 and 7 and their rejection are described in the above 103(a) rejection over Leskovar et al.

Claim 6 limits the pharmaceutical preparation comprising cis-platinum, oxaliplatinim or/and carboplatinum.

While Leskovar et al. teach the use of other DNA crosslinking compounds such as mitomycin C (Leskovar et al. paragraph 23) in a composition for cancer treatment he does not teach the specific use of DNA crosslinking agent cis-platinum. However Housman et al. teach that mitomycin C and cis-platinum are both DNA crosslinking agents (col 22, lines 14-15) and one of ordinary skill in the art would recognize them as common drugs for cancer treatment (col 21, line 55 to col 22, line 20). Therefore it

would be obvious to replace cis-platinum or other DNA crosslinking agents such as oxaliplatinum and carboplatinum since these are art-recognized equivalents for the same purpose (M.P.E.P. § 2144.06).

Therefore, the invention as a whole would have been prima facie obvious at the time of filing in view of the references listed above and as such claims 1-7 are not allowable.

In summary no claims, as written, are allowed for this application.

In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached during regular business hours, 8:00 to 17:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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